

CLAIMS

1. A process for preparing a glycopeptide having at least one asparagine-linked oligosaccharide at a desired position of the peptide chain thereof, the process comprising:

(1) esterifying a hydroxyl group of a resin having the hydroxyl group and a carboxyl group of an amino acid having amino group nitrogen protected with a fat-soluble protective group,

(2) removing the fat-soluble protective group to form a free amino group,

(3) amidating the free amino group and a carboxyl group of an amino acid having amino group nitrogen protected with a fat-soluble protective group,

(4) removing the fat-soluble protective group to form a free amino group,

(5) repeating the steps (3) and (4) at least once,

(6) amidating the free amino group and a carboxyl group of the asparagine portion of an asparagine-linked oligosaccharide having amino group nitrogen protected with a fat-soluble protective group,

(7) removing the fat-soluble protective group to form a free amino group,

(8) amidating the free amino group and a carboxyl group of an amino acid having amino group nitrogen protected with a fat-soluble protective group,

(9) repeating the steps (7) and (8) at least once,

(10) removing the fat-soluble protective group to form a free amino group, and

(11) cutting off the resin with an acid.

2. A process for preparing a glycopeptide having at least two asparagine-linked oligosaccharides at a desired position of the peptide chain thereof which comprises the process according to claim 1 wherein the steps (6) of amidating the free amino group and a carboxyl group of the asparagine portion of an asparagine-linked oligosaccharide having amino group nitrogen protected with a fat-soluble protective group, and (7) of removing the fat-soluble protective group to form a free amino group are additionally performed suitably.

3. A process for preparing a glycopeptide having at least one asparagine-linked oligosaccharide at a desired position of the peptide chain thereof according to claim 1 wherein the steps (6) of amidating the free amino group and the carboxyl group of the asparagine portion of an asparagine-linked oligosaccharide having amino group nitrogen protected with a fat-soluble protective group, and (7) of removing the fat-soluble protective group to form a free amino group are performed as final steps.

4. A process for preparing a glycopeptide according to claim 1 wherein the step (1) of esterifying a hydroxyl group of a resin having the hydroxyl group and a carboxyl group of the asparagine portion of an asparagine-linked oligosaccharide having amino group nitrogen protected with a fat-soluble protective group is performed in place of the step (6) or in addition to the step (6).

5. A process for preparing a glycopeptide according to claims 1 to 4 wherein the asparagine-linked oligosaccharide of the

step (6) of claim 1 has at least 6 sugar residues.

6. A process for preparing a glycopeptide according to claims 1 to 4 wherein the asparagine-linked oligosaccharide of the step (6) of claim 1 has 9 to 11 sugar residues.

7. A process for preparing a glycopeptide according to claims 1 to 4 wherein the asparagine-linked oligosaccharide of the step (6) of claim 1 has at least 6 sugar residues, and has a bifurcated oligosaccharide attached thereto.

8. A process for preparing a glycopeptide according to claims 1 to 4 wherein the asparagine-linked oligosaccharide in (6) is an asparagine-linked disialooligosaccharide or an asparagine-linked monosialooligosaccharide in which the carboxyl group of the
5 sialic acid is protected with a protective group.

9. A process for preparing a glycopeptide according to claims 1 to 4 wherein the asparagine-linked oligosaccharide in (6) is an asparagine-linked asialooligosaccharide.

10. A process for preparing a glycopeptide according to claim 8 wherein the protective group for the carboxyl group of the sialic acid is benzyl group.

11. A process for preparing a glycopeptide according to claims 1 to 4 wherein the fat-soluble protective group is 9-fluorenylmethoxycarbonyl (Fmoc) group.

12. A process for preparing a glycopeptide according to claims 1 to 11 wherein a mucin-linked oligosaccharide is used in place of a portion or the whole of the asparagine-linked oligosaccharide.

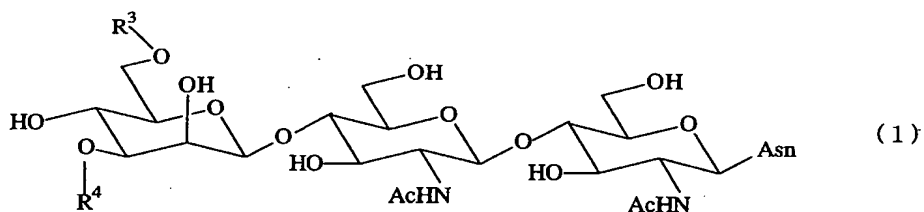
13. A glycopeptide which is obtainable by a process

according to claims 1 to 12 and which has at least one asparagine-linked oligosaccharide or mutin-linked oligosaccharide at a desired position of the peptide chain thereof.

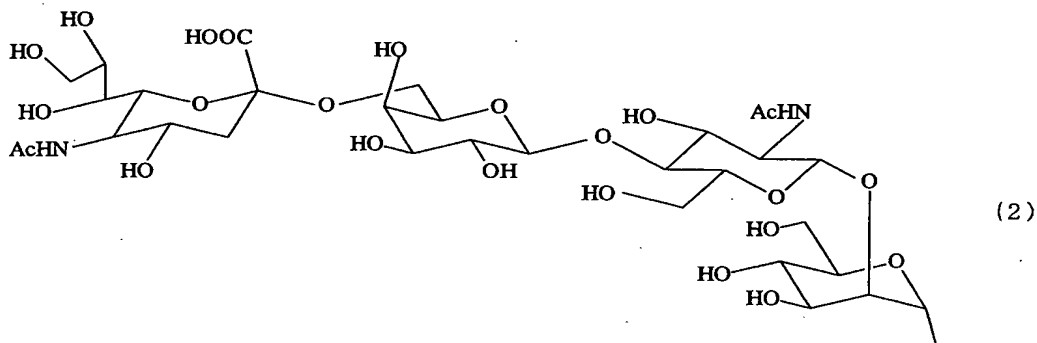
14. A glycopeptide according to claim 13 wherein the asparagine-linked oligosaccharide or the mutin-linked oligosaccharide has at least 6 sugar residues, and has a bifurcated oligosaccharide attached thereto.

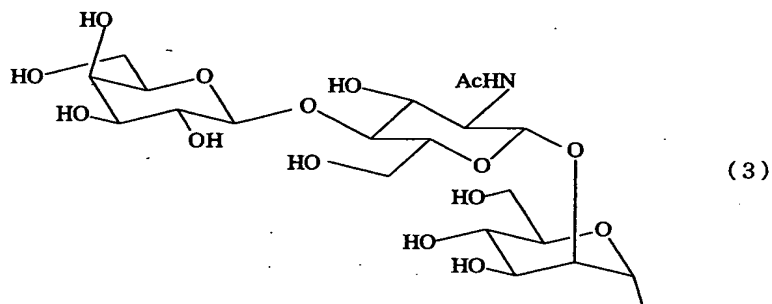
15. A glycopeptide according to claim 13 which is a glycopeptide having at least one oligosaccharide selected from among asparagine-linked disialooligosaccharide and asparagine-linked monosialooligosaccharide attached as the asparagine-linked
5 oligosaccharide.

16. A glycopeptide according to claim 13 wherein the asparagine-linked oligosaccharide is represented by the formula
(1)

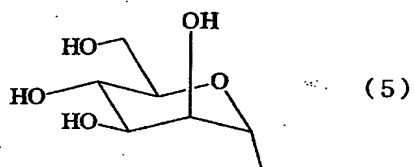
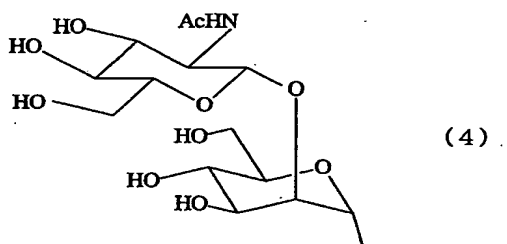


5 wherein R^3 and R^4 are each a hydrogen atom or a group represented by one of the formula (2) to (5), and may be the same or different.





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17. A process for preparing glycopeptide having at least one asparagine-linked oligosaccharide at a desired position of the peptide chain thereof and a residue of sialic acid or a derivative thereof at a terminal end thereof, the process comprising:

- 5 (1) esterifying a hydroxyl group of a resin having the hydroxyl group and a carboxyl group of an amino acid having amino group nitrogen protected with a fat-soluble protective group,
- (2) removing the fat-soluble protective group to form a free amino group,
- 10 (3) amidating the free amino group and a carboxyl group of an

amino acid having amino group nitrogen protected with a fat-soluble protective group,

(4) removing the fat-soluble protective group to form a free amino group,

15 (5) repeating the steps (3) and (4) at least once,

(6) amidating the free amino group and a carboxyl group of the asparagine portion of an asparagine-linked oligosaccharide having amino group nitrogen protected with a fat-soluble protective group,

(7) removing the fat-soluble protective group to form a free
20 amino group,

(8) amidating the free amino group and a carboxyl group of an amino acid having amino group nitrogen protected with a fat-soluble protective group,

(9) repeating the steps (7) and (8) at least once,

25 (10) removing the fat-soluble protective group to form a free amino group,

(11) cutting off the resin with an acid, and

(12) transferring sialic acid or a derivative thereof to the resulting glycopeptide using a sialic acid transferase.

18. A process for preparing a glycopeptide according to claim 17 wherein a marker is reacted with the resin before the resin is cut off with the acid in step (11).

19. A process for preparing a glycopeptide according to claim 18 wherein the marker is a dansyl halide.

20. A process for preparing 5-acetamido-3,5,7-trideoxy-7-fluoro-D-glycero- β -D-lacto-2-nonulopyranosidonic acid comprising reacting N-acetyl-4-deoxy-4-fluoro-D-mannosamine, sodium piruvate,

bovine serum albumin and aldolase sialate.

- 5 21. A process for preparing 5-acetamido-3,5,7-trideoxy-7-fluoro-D-glycero- β -D-lacto-2-nonulopyranosidonic acid comprising hydrogenating benzyl 2-azido-2,4-dideoxy-4-fluoro- β -D-mannopyranoside in the presence of acetic anhydride to obtain N-acetyl-4-deoxy-4-fluoro-D-mannosamine, and subsequently reacting
- 10 the product with sodium piruvate, bovine serum albumin and aldolase sialate.